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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/191,199	11/12/98	TANG	P 238/130

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EXAMINER	
COLEMAN, B	
ART UNIT	**PAPER NUMBER**
1624	27

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/191,199	TANG et al.
Examiner	**Art Unit**
Brenda Coleman	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 2, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-9, 11-16, 18-37, and 41-46* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-9, 11-16, 18-37, and 41-46* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s): *24, 25*

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Claims 1-9, 11-16, 18-37 and 41-46 are pending in the application.

Continued Prosecution Application

1. The request filed on September 18, 2000 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/191,199 is acceptable and a CPA has been established. An action on the CPA follows.

Election/Restriction

2. Applicant's election with traverse of Group I in Paper No. 13 is acknowledged. The traversal is on the ground(s) that it would not be a burdensome search. This is not found persuasive because first a heterocyclic moiety having a bicyclic ring system with nine ring atoms where at least one is a nitrogen atom is clearly a structurally dissimilar compound which is classified in various subclasses under classes 544 and 546 with respect to the number and position of the nitrogen atoms for which D, E, F and G may contain.

(1) Note MPEP 2173.05(h) "where a Markush expression is applied only to a portion of a chemical compound, the propriety of the grouping is determined by a consideration of the compound as a whole, and does not depend on there being a community of properties in the members of the Markush expression.

Therefore, what should be considered for patentable distinctness is the compound as a whole. Would a whole compound where D and F are nitrogen be patentably distinct from a whole compound where D is nitrogen? If a reference for one would not be a reference for the

other, then restriction is considered proper. Community of properties is not enough to keep 5,7-diaza-indoline and 4-aza-indoline in the same Markush claim, where the Markush expression is applied only to a portion of a chemical compound. It is the compound as a whole 5,7-diazaindoline vs 4-aza-indoline vs 7-aza-indoline, etc., that must be considered for patentable distinctness.

Thus, separate searches in the literature would be required. However, should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

(2) The degree of burden on the examiner is high. The class/subclass search on the elected invention where the compounds of formula I are an aza-indoline core would be as follows: class 514, subclass 300 and class 546, subclass 113 which involved 824 US patents. The classes and subclass mentioned above represent only the degree of burden within the U.S. Patent Classification System, this does not include the search required in the prior art of journal articles and foreign patents.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 42 and 43 are rejected as being drawn to an improper Markush group. The recited compounds, while possessing a common utility, differ widely in structure and are not art-recognized equivalents and are thus, independently distinct for the reasons set forth in the restriction above.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 19-37 and 46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims are not adequately enabled solely based on its protein tyrosine kinase inhibition provided in the specification. Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating seven types of cancer with members of a class of several compounds *In re Buting* 163 USPQ 689. The remarkable advances in chemotherapy have seen the development of specific compounds to treat specific types of cancer. The great diversity of diseases falling within the "tumor" category means that it is contrary to medical understanding that any agent (let alone a genus of thousands of compounds) could be generally effective against such diseases. The

intractability of these disorders is clear evidence that the skill level in this art is low relative to the difficulty of the task. Instant claim language embraces disorders not only for treatment but for **prevention** which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop lung cancer, prostate cancer, astrocytoma, breast cancer, etc. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

5. Claims 1-9, 11-16, 19-37 and 41-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment filed February 2, 2001, included the moiety "trihalomethane-carbonyl" in the definition of R^4, R^5, R^6, R^7, R^8, R^9 and R^{10}, which is not described in the specification with respect to formula 1.

Applicant is required to cancel the new matter in the reply to this Office action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-9, 11-16, 19-37 and 41-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a) Claims 1, 2, 11-16, 19-37 and 41-46 are vague and indefinite in that one of the substituents for R^{11}, is not valence satisfied, i.e. carbonyl.

b) Claims 1-9, 11-16, 19-37 and 41-46 are vague and indefinite in that two of the substituents for R^{12} and R^{13} at each occurrence are not valence satisfied, i.e. carbonyl and sulfonyl.

c) Claims 1-9, 11-16, 19-37 and 41-46 are vague and indefinite in that it is not known what is meant by the moiety in the definition of R^{12} and R^{13} at each occurence where combined they form a "five-six-member" heterocyclic ring.

d) Claims 1-9, 11, 19-37 and 41-46 are vague and indefinite in that one of the substituents for R^3, is not valence satisfied, i.e. carbonyl.

e) Claims 1-9, 11-16, 19-37 and 46 are vague and indefinite in that many of the substituents for R^4, R^5, R^6, R^7, R^8, R^9 and R^{10}, are not valence satisfied and/or defined as such in the specification that they include variables which are not defined within the claim, i.e. sulfinyl, S-Sulfonamido, N-Sulfonamido, carbonyl, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, guanyl, guanidino and ureido.

f) Claims 1-9, 11-16, 19-37 and 41-46 are vague and indefinite in that the list of substituents for the variables R^4, R^5, R^6, R^7, R^8, R^9 and R^{10}, includes amino which is embraced by $-NR^{12}R^{13}$ when R^{12} and R^{13} are hydrogen, and thus results in double inclusion. See Ex parte White 127 USPQ 261.

g) Claims 1 and 41 are vague and indefinite in that it is not known what is meant by O-thiocarbamyl, since thiocarbamyl does not contain an O atom.

h) Claims 4-9 recite the limitation "R2" in the claim. There is insufficient antecedent basis for this limitation in the claim.

i) Claim 5 is are vague and indefinite in that one of the substituents for R^7, R^8, R^9 and R^{10}, is defined as such in the specification that they include variables which are not defined within the claim, i.e. N-amido.

j) Claim 13 recites the limitation "C-carboxy" in the definition of R^4, R^5 and R^6. There is insufficient antecedent basis for this limitation in the claim.

k) Claim 13 recites the limitation "six-member cycloalkyl ring formed by the combination of R^4 and R^5" in the definition of R^4 and R^5. There is insufficient antecedent basis for this limitation in the claim.

l) Claims 20-37 and 46 are vague and indefinite in that the claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the diseases capable of being modulated by inhibiting the catalytic activity of protein tyrosine kinase. Determining whether a given disease responds or does not respond to such an inhibitor will involve undue experimentation. Suppose that a given drug, which has inhibitor properties *in vitro*, when administered to a patient with a certain disease, does not produce a

favorable response. One can not conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration can not be predicted in advance. Should our drug be given as a bolus *iv* or in a time release *po* formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active *in vitro*, simply is not potent enough or produces such low concentrations in the blood that it is not an

effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many different structurally related inhibitors must be tried before one concludes that a specific compound does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of whom are inhibitors *in vitro*, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property which the second drug is capable. It is common for a drug, particularly in cancer treatment, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were claimed to be a pure receptor XYX agonist or antagonist, but upon further experimentation shown to effect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some totally different drug. There are for example, agents in antiviral and anticancer chemotherapy which are not themselves

effective, but are effective treatments when the agents are combined with something else.

Consequently, determining the true scope of the claim will involve extensive and potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

m) Claims 41, 44 and 45 are vague and indefinite in that it is not known what is meant by the variable E in formula 2. There is no definition in the claim for variable E.

n) Claims 41, 44 and 45 are vague and indefinite in that the definition of the variable F appears twice.

o) Claims 41, 44 and 45 are vague and indefinite in that many of the substituents for R^7, R^8, R^9 and R^{10}, are not valence satisfied and/or defined as such in the specification that they include variables which are not defined within the claim, i.e. sulfinyl, S-Sulfonamido, N-Sulfonamido, carbonyl, N-amido, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, guanyl, guanidino and ureido.

p) Claims 41, 44 and 45 are vague and indefinite in that it is not known what is meant by the "and" which appears before trihalomethanesulfonyl in the definition of R^{11}, indicating the end of the claim which is not so.

q) Claims 41, 44 and 45 are vague and indefinite in that it is not known what is meant by the "when-B" in the definition of B for formula 3.

r) Claims 41, 44 and 45 are vague and indefinite in that many of the substituents for R^4, R^5 and R^6, are not valence satisfied and/or defined as such in the specification that they include variables which are not defined within the claim, i.e. sulfinyl, S-Sulfonamido, N-Sulfonamido, carbonyl, N-amido, O-carbamyl, N-carbamyl, O-thiocarbamyl, N-thiocarbamyl, guanyl, guanidino and ureido.

s) Claim 42 is vague and indefinite in that it is not known what is meant by "an azaindolin-2-oneselected".

t) Claim 42 recites the limitation "2-methoxycarbonylethyl" in the species of line 7 on page 10, line 3 on page 15, line 13 on page 16, line 22 on page 17, line 27 on page 18, line 3 on page 20, line 19 on page 21, line 29 on page 22. There is insufficient antecedent basis for this limitation in the claim.

u) Claim 42 recites the limitation "1-methylbenzimidazol" in the species of line 1 on page 11, line 6 on page 15, line 16 on page 16, line 24 on page 17, line 29 on page 18, line 6 on page 20, line 22 on page 21, line 1 on page 23. There is insufficient antecedent basis for this limitation in the claim.

v) Claim 42 recites the limitation "4,5,6,7-tetrahydroindol" in the species of line 3 on page 11, line 7 on page 15, line 17 on page 16, line 26 on page 17, line 31 on page 18, line 8 on page 20, line 24 on page 21, line 3 on page 23. There is insufficient antecedent basis for this limitation in the claim.

w) Claim 42 recites the limitation "thieno[2,3-b]thien" in the species of line 5 on page 11, line 11 on page 15, line 20 on page 16, line 28 on page 17, line 2 on page 19, line 12 on page 20, line 27 on page 21, line 6 on page 23. There is insufficient antecedent basis for this limitation in the claim.

x) Claim 42 recites the limitation "**trifluoro**-1-(thien-2yl)**ethylidenyl**" in the species of line 13 on page 11, line 19 on page 15, line 28 on page 16, line 5 on page 18, line 10 on page 19, line 22 on page 20, line 4 on page 22, lines 14-15 on page 23. There is insufficient antecedent basis for this limitation in the claim.

y) Claim 42 recites the limitation "benzyl" in the species of line 20 on page 11, line 27 on page 15, line 5 on page 17, line 12 on page 18, line 17 on page 19, line 1 on page 21, line 12 on page 22, line 23 on page 23. There is insufficient antecedent basis for this limitation in the claim.

z) Claim 42 recites the limitation "acetyl" in the species of line 21 on page 11, line 29 on page 15, line 7 on page 17, line 13 on page 18, line 18 on page 19, line 3 on page 21, line 14 on page 22, line 25 on page 23. There is insufficient antecedent basis for this limitation in the claim.

aa) Claim 42 recites the limitation "methoxycarbonylmethyl" in the species of line 23 on page 11, line 30 on page 15, line 9 on page 17, line 15 on page 18, line 20 on page 19, line 4 on page 21, line 15 on page 22, line 27 on page 23. There is insufficient antecedent basis for this limitation in the claim.

ab) Claim 42 recites the limitation "chlorobenzoyl" in the species of line 24 on page 11, line 31 on page 15, line 10 on page 17, line 16 on page 18, line 21 on page 19, line 6 on page 21, line 16 on page 22, line 28 on page 23. There is insufficient antecedent basis for this limitation in the claim.

ac) Claim 42 recites the limitation "5-(trifluoromethyl)pyrrol" in the species of line 25 on page 11, line 1 on page 16, line 11 on page 17, line 17 on page 18, line 22 on page 19, line 7 on page 21, line 17 on page 22, line 29 on page 23. There is insufficient antecedent basis for this limitation in the claim.

ad) Claim 42 recites the limitation "3-(trifluoromethyl)pyrrol" in the species of line 26 on page 11, line 3 on page 16, line 12 on page 17, line 18 on page 18, line 23 on page 19, line 8 on page 21, line 19 on page 22, line 30 on page 23. There is insufficient antecedent basis for this limitation in the claim.

ae) Claim 42 recites the limitation "4-phenylethynyl" in the species of line 27 on page 11, line 4 on page 16, line 14 on page 17, line 19 on page 18, line 24 on page 19, line 10 on page 21, line 20 on page 22, line 1 on page 24. There is insufficient antecedent basis for this limitation in the claim.

af) Claim 42 recites the limitation "2-phenylethynyl" in the species of line 28 on page 11, line 5 on page 16, line 15 on page 17, line 20 on page 18, line 25 on page 19, line 11 on page 21, line 21 on page 22, line 2 on page 24. There is insufficient antecedent basis for this limitation in the claim.

ag) Claim 42 recites the limitation "benzothien" in the species of line 29 on page 11, line 6 on page 16, line 15 on page 17, line 21 on page 18, line 26 on page 19, line 12 on page 21, line 22 on page 22, line 3 on page 24. There is insufficient antecedent basis for this limitation in the claim.

ah) Claim 42 recites the limitation "carboxyethyl" in the species of line 30 on page 11, line 7 on page 16, line 16 on page 17, line 22 on page 18, line 27 on page 19, line 13 on page 21, line 23 on page 22, line 4 on page 24. There is insufficient antecedent basis for this limitation in the claim.

ai) Claim 42 recites the limitation "5,7-diaza" in the species spanning line 30 on page 11 to line 28 on page 14. There is insufficient antecedent basis for this limitation in the claim.

aj) Claim 42 recites the limitation "5-acetamido" in the species spanning line 24 on page 22 to line 5 on page 24. There is insufficient antecedent basis for this limitation in the claim.

ak) Claim 43 recites the limitation "2-methoxycarbonylethyl" in the species of line 13 on page 24, line 17 on page 28, line 27 on page 29, line 5 on page 31, line 10 on page 32, line 17 on page 33, line 2 on page 35, line 12 on page 36. There is insufficient antecedent basis for this limitation in the claim.

al) Claim 43 recites the limitation "1-methylbenzimidazol" in the species of line 15 on page 24, line 20 on page 28, line 30 on page 29, line 7 on page 31, line 12 on page

32, line 20 on page 33, line 5 on page 35, line 15 on page 36. There is insufficient antecedent basis for this limitation in the claim.

am) Claim 43 recites the limitation "4,5,6,7-tetrahydroindol" in the species of line 17 on page 24, line 21 on page 28, line 31 on page 29, line 9 on page 31, line 14 on page 32, line 22 on page 33, line 7 on page 35, line 17 on page 36. There is insufficient antecedent basis for this limitation in the claim.

an) Claim 43 recites the limitation "thieno[2,3-b]thien" in the species of line 19 on page 24, line 25 on page 28, line 3 on page 30, line 11 on page 31, line 16 on page 32, line 26 on page 33, line 10 on page 35, line 20 on page 36. There is insufficient antecedent basis for this limitation in the claim.

ao) Claim 43 recites the limitation "**trifluoro**-1-(thien-2yl)**ethylidenyl**" in the species of line 27 on page 24, line 2 on page 29, line 11 on page 30, line 19 on page 31, line 24 on page 32, line 5 on page 34, line 18 on page 35, lines 28-29 on page 36. There is insufficient antecedent basis for this limitation in the claim.

ap) Claim 43 recites the limitation "benzyl" in the species of line 3 on page 25, line 10 on page 29, line 19 on page 30, line 26 on page 31, line 31 on page 32, line 15 on page 34, line 26 on page 35, line 6 on page 37. There is insufficient antecedent basis for this limitation in the claim.

aq) Claim 43 recites the limitation "acetyl" in the species of line 4 on page 25, line 12 on page 29, line 21 on page 30, line 27 on page 31, line 1 on page 33, line 17 on

page 34, line 28 on page 35, line 8 on page 37. There is insufficient antecedent basis for this limitation in the claim.

ar) Claim 43 recites the limitation "methoxycarbonylmethyl" in the species of line 6 on page 25, line 13 on page 29, line 23 on page 30, line 29 on page 31, line 3 on page 33, line 18 on page 34, line 29 on page 35, line 10 on page 37. There is insufficient antecedent basis for this limitation in the claim.

as) Claim 43 recites the limitation "chlorobenzoyl" in the species of line 7 on page 25, line 14 on page 29, line 24 on page 30, line 30 on page 31, line 4 on page 33, line 20 on page 34, line 30 on page 35, line 11 on page 37. There is insufficient antecedent basis for this limitation in the claim.

at) Claim 43 recites the limitation "5-(trifluoromethyl)pyrrol" in the species of line 8 on page 25, line 15 on page 29, line 25 on page 30, line 31 on page 31, line 5 on page 33, line 21 on page 34, line 31 on page 35, line 12 on page 37. There is insufficient antecedent basis for this limitation in the claim.

au) Claim 43 recites the limitation "3-(trifluoromethyl)pyrrol" in the species of line 9 on page 25, line 17 on page 29, line 26 on page 30, line 1 on page 32, line 6 on page 33, line 22 on page 34, line 2 on page 36, line 13 on page 37. There is insufficient antecedent basis for this limitation in the claim.

av) Claim 43 recites the limitation "4-phenylethynyl" in the species of line 10 on page 25, line 18 on page 29, line 28 on page 30, line 2 on page 32, line 7 on page 33,

line 24 on page 34, line 3 on page 36, line 15 on page 37. There is insufficient antecedent basis for this limitation in the claim.

aw) Claim 43 recites the limitation "2-phenylethynyl" in the species of line 11 on page 25, line 19 on page 29, line 29 on page 30, line 3 on page 32, line 8 on page 33, line 25 on page 34, line 4 on page 36, line 16 on page 37. There is insufficient antecedent basis for this limitation in the claim.

ax) Claim 43 recites the limitation "benzothien" in the species of line 12 on page 25, line 20 on page 29, line 29 on page 30, line 4 on page 32, line 9 on page 33, line 26 on page 34, line 5 on page 36, line 17 on page 37. There is insufficient antecedent basis for this limitation in the claim.

ay) Claim 43 recites the limitation "carboxyethyl" in the species of line 13 on page 25, line 21 on page 29, line 30 on page 30, line 5 on page 32, line 10 on page 33, line 27 on page 34, line 6 on page 36, line 18 on page 37. There is insufficient antecedent basis for this limitation in the claim.

az) Claim 43 recites the limitation "5,7-diaza" in the species spanning line 14 on page 25 to line 11 on page 28. There is insufficient antecedent basis for this limitation in the claim.

ba) Claim 43 recites the limitation "5-acetamido" in the species spanning line 7 on page 36 to line 19 on page 37. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al., WO 96/16964 (US equivalent 5,719,135). The generic structure of US '135 encompasses the compounds of the instant invention (see Formula I, column 1) and the process of preparing the compounds as claimed herein. Examples 53-71, etc. differ only in the nature of the R_1, R_2, R_3, q and A substituents. Column 1, lines 23 through column 2, line 8 defines the substituent A as benzene, naphthalene, 5,6,7,8-tetrahydronaphthalene, quinoline, isoquinoline, indole or 7-azaindole; R_1 as -H, -CN, $-SO_3R_4$, $-SO_2NHR_5$, etc.; R_2 as C_1-C_6 alkyl, halogen, or hydroxy; R_3 as -H or C_1-C_6 alkyl; and q as zero, 1 or 2. Compounds of the instant invention are generically embraced by US '135 in view of the interchange ability of R_1, R_2, R_3, q and A substituents of the azaindolin-2-one ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example A is indole as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

8. Claims 41-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buzzetti et al., WO 96/16964 (US equivalent 5,719,135). The generic structure of US '135 encompasses the compounds of the instant invention (see Formula I, column 1) and the process of preparing the compounds as claimed herein. Examples 53-71 of US '135 are position isomers of the compounds of the instant invention where compounds such as compound 52 in column 4 has the A variable attached at the 3-position of the indolyl ring attached to the azaindolin-2-one ring through methenylene. One of ordinary skill in the art at the time the invention was made would have been motivated to substitute the instantly claimed isomer for the known tyrosine kinase inhibitors of US '135. Such modification would be obvious because such structurally related compounds suggest one another and would be expected to share common properties absent a showing of unexpected results. (See In re Norris, 84 USPQ 459, on the obviousness of structural isomers).

9. Claims 1-9, 11-16, 18-37 and 41-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al., U.S. Patent No. 6,147,106. The generic structure of US '106 encompasses the instantly claimed compounds (see Formula III, column 6) as claimed herein. The examples in Tables 95, 10, etc. differ only in the nature of the A_1, A_2, A_3 and A_4 substituents. Column 6, lines 35-36 defines the substituents A_1, A_2, A_3 and A_4 as independently carbon or nitrogen. Compounds of the instant invention are generically embraced by US '106 in view of the interchange ability of A_1, A_2, A_3 and A_4 substituents of the azaindolin-2-one ring system.

one of ordinary skill in the art at the time the invention was made would have been motivated to select for example A_1 is nitrogen and A_2, A_3 and A_4 are carbon as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays and Tuesdays from 9:00 AM to 3:00 PM and from 5:30 PM to 7:30 PM and on Wednesday thru Friday from 9:00 AM to 6:00 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brenda Coleman

Brenda Coleman
Primary Examiner AU 1624
October 16, 2001